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EXAMINER

SHEINBERG, MONIKA B

ART UNIT PAPER NUMBER

1631

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/671,817

Applicant(s)

EDWARDS ET AL.

Examiner

Monika B Sheinberg

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 June 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-66 is/are pending in the application.
- 4a) Of the above claim(s) 4,6-37,44-57,65 and 66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,38-43 and 58-64 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-66 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,11.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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**DETAILED ACTION*****Election/Restrictions***

Applicant's election with traverse of Group III (claims 1-43 and 58-64) in Paper No. 10 filed: 13 June 2002, is acknowledged. The traversal is on the ground(s) that ~~Groups I, II and IV~~ include the same subject matter of Group III, thus would not be a search burden for the examiner. This is not found persuasive because although the initial steps of the methods may be similar, the steps of methodology do not require the same protocols; for example the experimental procedures for determining the structure of a protein as required of claim 44, and the experimental procedures for purifying protein as required of claim 51 are different than those experimental procedures for determining protein expression. The purification of a protein does not require modification of how a protein structure is determined and vice versa. The experimental procedures of drug-target discovery required optimization towards a desired property for a drug that passes a designated threshold of criteria sets. Thus the Groups are patentably distinct due to different steps requiring different methods of science and technology.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of species solubility for the biochemical or biophysical property in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the species election, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 4, 6-37, 44-57, 65 and 66 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claims 1-66 are pending. Claims 1-3, 5, 38-43 and 58-64 have been examined.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, 38, 40-43, 58, 59 and 61-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the decision-tree analysis for the data-mining technique, does not reasonably provide enablement for any data-mining technique. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to perform the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant application fails to provide guidance to one of ordinary skill in the art for performing data-mining techniques other than decision-tree analysis. The specification does not provide or suggest how to perform data-mining techniques other than that of decision-tree analysis for database analysis of biophysical or biochemical properties thus not enabling one of ordinary skill in the art to know how utilize such methods as case-based reasoning, Bayesian classifier, simple linear discriminant analysis and support vector machines as recited in claims 38, 40-43, 59 and 61-64.

The specification on page 9 (2<sup>nd</sup> paragraph) is generic in nature and fails to teach or suggest how other data-mining techniques are to be practiced with the methods of claim 1 or claim 58. Example III teaches decision-tree analysis with the aide of Figure 1 of the specification. However, neither Example III nor the other examples provide a description of how to perform any data-mining techniques other than by decision-tree analysis. While working examples are not, per se, required, the specification must provide adequate guidance such that

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one of skill in the art could practice the invention without undue experimentation. Given the lack of descriptive working examples in the specification, and the unpredictability of data-mining techniques for determining biochemical or biophysical properties of a protein sequence, the specification, as filed is not enabling for any method of data-mining as claimed other than that of decision-tree analysis.

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Claims 58-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant application fails to provide guidance to one of ordinary skill in the art for modifying experimental procedures or modifying protein sequence for optimizing high-throughput protein expression as seen in claim 58. The specification does not provide or suggest what are the modifications of experimental procedures or protein sequences specific for high-throughput optimization thus not enabling one of ordinary skill in the art to know how optimize the method described. The specification on page 9 (lines 19-20) states that the "nature of the invention allows one to preemptively adjust experimental condition to optimize, for example, [...] protein expression techniques" in a generic sense without any disclosure as to how this modification is performed particularly for high-throughput optimization. Nowhere are the modifications to protein sequence described in regards to high-throughput protein expression.

The examples provided are only a generic description of the claimed method. None of the examples provide a description of how to perform the modifications specific to high-throughput practice. The "Expression Strategy" of Example I on page 15 is brief and generic stating, "a single set of growth conditions optimized for the majority of proteins" was utilized for throughput practice. The use of a single set does not provide a demonstration of procedural modification for optimizing throughput. This section does not demonstrate the modification of protein sequences at all. Optimization is demonstrated in regards to purification, crystallization or NMR, on pages 15-16, however not in regards to protein expression as required by claim 58. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of descriptive working examples in the specification, and the unpredictability of protocol modification or protein sequence modification for high-throughput practices, the specification, as filed is not enabling for the method of modifying experimental procedures or modifying protein sequences for optimizing high-throughput protein expression as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 38-43 and 58-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 is vague and indefinite due to the lack of clarity in the claim language of step (c) "correlating [...], and". It is unclear what the action of correlation is between. Claims 2, 3, 5 and 38-43 are also indefinite due to dependency from claim 1.

Claims 1 and 58 are vague and indefinite due to the lack of clarity in the term "protein sequence information" line 3 of both claims. The metes and bounds of the parameters of that which defined "information" is unclear. Claims 2, 3, 5, 38-43 and 59-64 are also indefinite due to dependency from claims 1 and 58.

Claims 1 and 58 are vague and indefinite due to the lack of clarity in the database provided in step (a). The metes and bounds of the contents of the database are unclear; for example, if the information is limited to one genome species such as *Methanobacterium thermoautotrophicum* as seen in Example I, or a plethora of various protein sequences derived from various sources/genomes. It is unclear if the database includes the protein of interest recited in the preamble, or if the database only comprises other proteins. For example it is unclear if the database comprises protein sequence information of the protein of interest stated in the preamble, or if the information concerns other protein sequences that are known. The same is true for the biophysical or biochemical properties. Claims 2, 3, 5, 38-43 and 59-64 are also indefinite due to dependency from claims 1 and 58.

Claims 1 and 58 are vague and indefinite due to the lack of clarity in the analysis step (b). The method step indicates the database is being analyzed yet does not indicate the objective of the analysis. It is unclear as to what are the metes and bounds of the parameters for analysis of the database or the individual entries of interest. In addition, the analysis of step (b) of the instant claims may be meant to result in the “correlating” of step (c) (claim 1), or “determining correlations” (claim 58). If the latter is intended, then the claims are not clear that the correlating or correlations are the result of the analysis of step (b). Claims 2, 3, 5, 38-43 and 59-64 are also indefinite due to dependency from claims 1 and 58.

Claim 3 is vague and indefinite due to the lack of clarity of the claim language “results obtained from” (i.e. claim 3, lines 5-6). It is unclear what the metes and bounds of the parameters that define any possible data or “results” that may result from the listed techniques (i.e. fluorescence). An added unclarity is that the claim in line 1 lists possible biophysical properties that confusingly are not “results” as in line 5. For example it is unclear how a result of nuclear magnetic resonance is a property. Claim 5 is also indefinite due to dependency from claim 3.

Claim 58 recites the limitation “the experimental procedures” in line 11. There is no antecedent basis for this limitation in the claim. Claims 59-64 are also indefinite due to dependency from claim 58.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 38 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Payne et al (*Nuc. Acids Res.*, 1997).

Payne et al demonstrates a proteomic yeast database of *Saccharomyces cerevisiae* that includes protein sequence information and protein property information such as “functions, [...] physical interactions, domain structures [...] similarities to other proteins” (p. 57, 1<sup>st</sup> column, last paragraph) as required by claim 1. The database includes analysis tools for data mining, maintained by Martins-Reid Institute for Protein Sequences (p. 57, 2<sup>nd</sup> column, 1<sup>st</sup> paragraph). A data mining technique such as the decision tree analysis as seen in claims 38 and 39, is demonstrated by simple decision-making analysis tools deciding what correlations exist, or not, between protein biophysical properties and sequence data. Each yeast protein has an entry that correlates protein biophysical or biochemical properties (claim 2) with the sequence data entered, with links to sequence databases such as “GenBank, PIR-International and SWISS-PROT” (2<sup>nd</sup> column, 1<sup>st</sup> paragraph). The reference points to biophysical properties such as solubility (Figures 2 and 3) as recited in claim 3 and 5. Thus Payne et al anticipates the instant claims.

### ***Conclusion***

No claim is allowed.

### ***Inquiries***

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can



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normally be reached on Monday-Friday from 9 A.M. to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

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September 30, 2002

Monika B. Sheinberg  
Art Unit 1631

*MBS*

*Ardin H. Marschel*  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER